

to the dust and fumes of a large foundry (Groups 3 and 4). The highest prevalence of bronchitis was among the men with silicosis.

As in previous studies, the adverse effect of cigarette smoking is well demonstrated, with a marked increase in prevalence in the moderate and heavy smokers.

The spirogram shows the expected decline with age in all parameters of ventilation. The presence of bronchitis did not result in any greater decay in ventilation over the 6-year period, although the bronchitic men initially had a lower mean value in most cases.

I might anticipate some of the discussion of this paper by pointing out differences between this study and some of those reported from England. For the most part, the English worker lives near his place of employment and is, therefore, subjected throughout 24 hours of the day to much the same environmental pollution, whereas most of the Detroit group have cars and live in areas remote from the plant and may therefore be exposed to significant air pollution only during the working day of 8-10 hours. Furthermore, the English studies are mainly composed of homogeneous ethnic groups, whereas the Detroit group is composed of many racial strains including Negroes, European immigrants, and American-born whites. For these reasons, it is difficult to make any direct comparisons between English studies and this study from Detroit.

In conclusion, we would again emphasize the importance of not transferring the findings in specially selected population groups to the general population.

THE BRONCHIAL AND EMPHYSEMATOUS TYPES OF CHRONIC OBSTRUCTIVE LUNG DISEASE IN LONDON AND CHICAGO

Benjamin Burrows, M.D.

A number of investigators have attempted to identify different clinical types among the diverse group of patients with chronic airways obstruction, and some have attempted to relate differences in clinical manifestations to the relative severity of anatomical emphysema and chronic bronchitis.¹⁻⁷ I hope that the current investigation will help tie together some of these observations. I also hope it will confirm a relationship of clinical and pathological findings and will further characterize two different clinical forms of chronic airways obstruction.

The present study dates from 1961, when Dr. Charles Fletcher and I undertook a comparative study of patients with irreversible airways obstruction in his chronic bronchitis clinic in London and in our emphysema clinic in Chicago. There was little difference in the clinical, radiological, and physiological findings for patients from opposite sides of the Atlantic, but it was evident that there was considerable individual variation among the patients in both of the clinics.^{8,9} Two distinct clinical types seemed to be apparent (see table 1).

Our findings suggested that one group of patients (table 1, type A findings) might have severe anatomical emphysema, while a second group (table 1, type B findings) might have a primarily inflammatory or bronchitic type of syndrome. However, at that time, the autopsy data were insufficient to confirm the theory that groupings of clinical findings reflected different underlying anatomical abnormalities. Indeed, even the statistical validity of the separation of two clinical types was somewhat questionable. We have since explored the statistical problem in a larger group of patients in Chicago. And these studies indicate that the various features of type A and type B disease are significantly intercor-

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related. Also, when data on 175 Chicago patients were subjected to a multiple factor analysis, the first factor picked out by computer contained the features of the type A patient, and the second factor contained features of the type B, as shown in the following table.

RESULTS OF MULTIPLE FACTOR ANALYSIS

Factor 1	Factor 2
Little sputum	Copious sputum
Mucoid sputum	Purulent sputum
Large total lung capacity	Small total lung capacity
Normal arterial CO ₂	High arterial CO ₂
Small cardiac shadow	Large cardiac shadow
Low diffusing capacity	Normal diffusing capacity
Quiet chest	Noisy chest
Normal serum globulin	High serum globulin
Underweight	Normal weight
X-ray emphysema	X-ray "inflammatory change"

Severity of expiratory slowing and of dyspnea was positively correlated with both factors. Although this does not prove the existence of the two syndromes, it has advantages over hand grouping of the data in removing bias and allowing a greater number of parameters to be examined simultaneously. It is of interest that a high serum globulin and noisy chest were associated with type B features, while weight loss was associated with type A. Also, typical patterns of either type were associated with more severe degrees of expiratory slowing and dyspnea.

Clinico-Pathological Studies

It took somewhat longer to demonstrate that these two types of disease occurred in patients with different anatomical alterations in their lungs.

As already reported in more detail,¹⁰ 32 lungs (15 from London and 17 from Chicago) were obtained from patients who were enrolled in prospective clinical studies in the two countries and were fixed in distension. These patients had all been studied during a stable stage in their disease between 6 months and 3 years prior to death. In most cases, the last research evaluation was within 18 months of demise. When more than one such evaluation was available for a single patient, average values were used in the analysis. Data obtained during exacerbations of disease and during the terminal illness were excluded. Lungs were graded for severity of emphysema on a 0-18 scale by Drs. B.E. Heard and J.S. Wootliff, pathologists at Hammersmith Hospital in London. They had no knowledge of the corresponding clinical or physiological data.

CLINICAL STUDIES

TABLE 1.—Two distinct clinical types

Examination	Type A	Type B
Chest X-ray	Often radiological evidence of emphysema.	Often radiological evidence of inflammatory disease. Usually >10 ml./day and often purulent. Often slight.
Sputum	Usually scanty and mucoid. Usually marked	Often normal or only slightly low. Common when expiratory slowing severe. Frequent. Occasional.
Pulmonary overdistention.	Usually markedly reduced.	
Breath-holding diffusing capacity.	Uncommon	
Chronic hypercapnia	Uncommon	
Chronic cor pulmonale ..	Rare	
Polycythemia		

There was no significant difference between the severity of anatomical emphysema in British and American lungs; the mean grades were 5.9 and 6.0, respectively. However, as seen in table 2, the pooled series showed significant correlations between the extent of anatomical emphysema and various clinical and physiological data. Radiological emphysema was found only in patients with 10 or more units of anatomical emphysema; it occurred in 6 of 10 such patients. Sputum production and diffusing characteristics were almost as useful in predicting the severity of anatomical emphysema. The total lung capacity, which had only a questionable significant overall correlation, was less than predicted in 7 of 10 patients with 5 units or less of anatomical emphysema but in only 5 of 22 patients with more emphysematous lungs was it less than predicted.

The relationship of anatomical emphysema to carbon dioxide tension is particularly striking, especially if the latter is expressed as deviation from predicted. A formula for predicting carbon dioxide tension from the FEV₁, previously derived from data on a larger group of patients,¹¹ was used in the present study to calculate a predicted carbon dioxide tension for each patient. In figure 1, deviation from predicted Pco₂ is plotted against emphysema grade; the correlation coefficient is -0.71 (P<.001).

Because the prediction of anatomical emphysema from clinical and physiological data can be made more accurate by simultaneous consideration of two or more variables, several equations were derived by multiple regression techniques. An example of such an equation is

$$\text{Predicted emphysema} = 7.8 - 3.3S + 4.4R - 0.1D$$

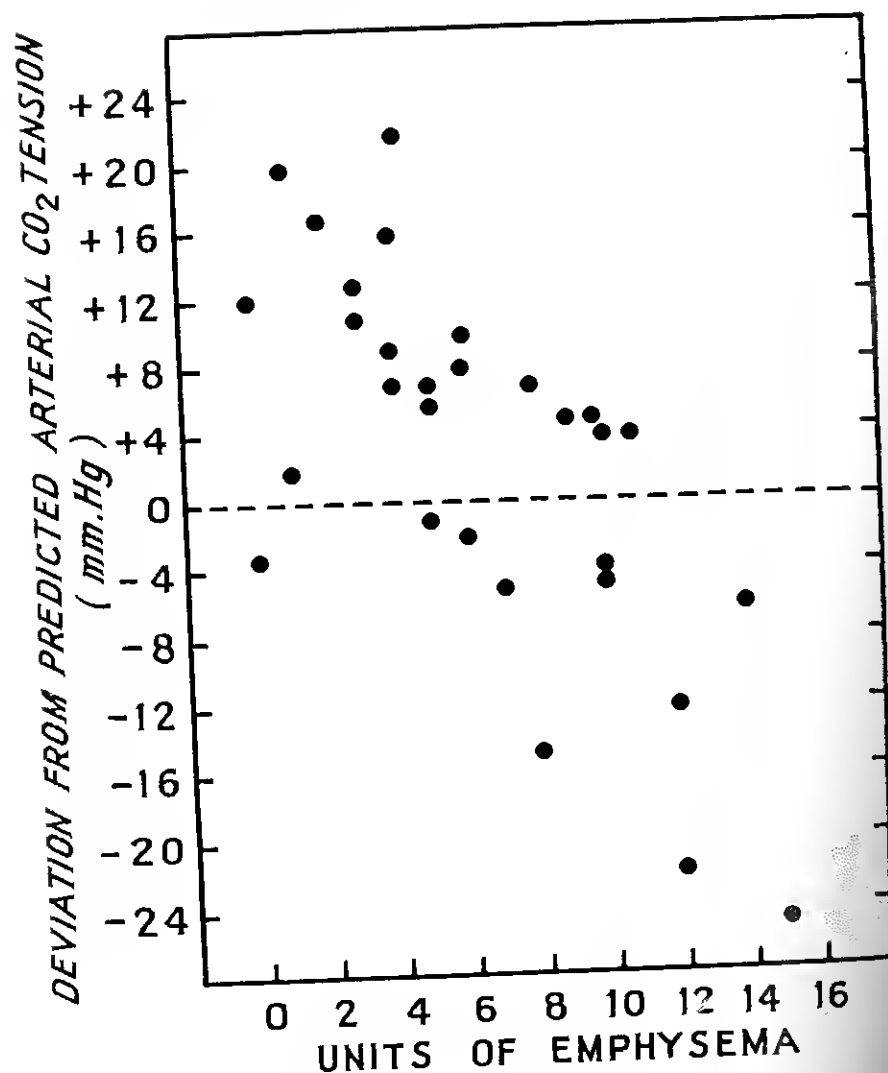


FIGURE 1. Anatomical emphysema versus deviation from predicted P_{CO_2} .

where S is 1 if more than 10 ml. of sputum is produced each day, S is 0 if there are lesser volumes; R is 1 if there is definite radiological emphysema, R is 0 without this X-ray finding; and D is the deviation from predicted P_{CO_2} expressed in mm. hg. Using this equation, predicted and observed emphysema had a correlation coefficient of 0.85 in the present study.

Since this type of equation is not readily applicable to clinical practice, some relatively simple criteria have been determined

which tend to separate the most emphysematous patients from the least emphysematous patients. These are presented in the following table listing our criteria for separating patients with chronic airways obstruction according to severity of anatomical emphysema:

Type A disease

(Severe emphysema—"emphysematous type"):

1. Definite attenuation of the peripheral vascular pattern on chest X-ray without concomitant inflammatory change.
- or—
2. A normal chest X-ray without the hypercapnia, the reduced total lung capacity, or the well-preserved diffusing capacity characteristic of type B patients.

Type B disease

(Absence of or mild emphysema—"bronchial type"):

No radiological evidence of emphysema and at least three of the following:

1. Persistently > 10 milliliters of sputum daily.
2. Arterial CO_2 tension 6 millimeters or above the level predicted from the FEV₁.
3. Definite X-ray evidence of chronic inflammatory disease in the lung parenchyma.
4. Total lung capacity less than predicted.
5. A single breath diffusing capacity per liter of lung volume of 3.5 or more.
6. Chronic or recurrent heart failure due to persistent cor pulmonale.

Type X disease (indeterminate):

Failure to fulfill criteria for either type A or B.

The preceding criteria closely resemble criteria used earlier for distinguishing different clinical types of disease. The anatomical findings in groups determined by these criteria are shown in figure 2. There is little overlap of anatomical findings in types A and B, and the intermediate type X shows an intermediate grade of emphysema. However, anatomical distinctions are only quantitative. Dr. Heard could detect no significant difference in the type of emphysema in the three groups.

An interesting observation was the tendency for heart weight to be inversely related to severity of emphysema. In our own data, this correlation was only questionably significant, but when the number of observations was increased by combining our data with those of Cromie,¹² the negative correlation becomes highly significant ($r = .46$, $P < .001$). There was a lower order but still significant negative correlation between right ventricular thickness and anatomical emphysema.

Using the criteria in the preceding table, we classified the 100 patients in the original London-Chicago study as types A and B

TABLE 2.—Correlations with grade of anatomical emphysema

Grade of emphysema	Correlation coefficient	Probability
Radiological emphysema	+ .70	< .001
Consistently >10 milliliters of sputum a day....	— .63	< .001
Arterial carbon dioxide tension.....	— .62	< .001
Breath-holding diffusing capacity ¹	— .61	< .001
Radiological "inflammatory" change	— .45	< .01
Chronic congestive heart failure	— .44	< .01
Total lung capacity (percent predicted).....	+ .33	= .05

¹ Expressed as diffusing capacity per liter of lung volume.

or X, and compared clinical courses of these groups. Over a 3-year period, patients in the two countries (England and the United States) died at nearly identical rates (about 9 percent a year), but in both countries, patients with type B disease (bronchial type) had a higher mortality than patients with other types of illness. This excess mortality appeared to be explained entirely by the higher CO₂ tensions of type B patients, both the severity of expiratory slowing and the degree of hypercapnia being important predictors of mortality. This prediction of mortality could not be improved by including other variables in the study. Except for the differences in death rate, no meaningful differences in the courses of types A and B were noted. Serial changes in symptoms, clinical findings, and physiological tests were similar in the two groups.

Ventilatory Mechanics and Mechanisms of CO₂ Retention

Additional studies were carried out in Chicago in an attempt to explain the greater tendency toward carbon dioxide retention in patients with the bronchial type B disease. (These studies have now been reported in detail.¹³)

Some of the observations confirm the earlier work of Kahana,¹⁴ Gilbert,¹⁵ and their colleagues and that of Park.¹⁶ Studies to be presented may help tie together some of the features of the different clinical syndromes just described.

A group of 34 patients enrolled in a prospective study of chronic obstructive lung disease underwent ventilatory and lung mechanics studies. Tests were performed with patients resting in a sitting position. Pulmonary resistance and dynamic compliance meas-

TABLE 3.—Correlation of ventilatory parameters with CO₂ tension

Ventilatory parameters	Correlation coefficient	Probability
Minute volume		
1/tidal volume	— .36	< .05
Respiratory frequency	+ .72	< .001
Physiological dead space	+ .56	< .001
Percentage of physiological dead space ventilation.....	— .41	< .05
Percentage of anatomical dead space ventilation. ¹	+ .65	< .001
Percentage of alveolar dead space ventilation ¹ .	+ .72	< .001
Percentage of alveolar dead space ventilation ¹ .	Not significant.	

¹ Calculated by assuming an anatomical dead space of 175 milliliters.

urements were made with the esophageal balloon method. Mixed venous carbon dioxide tensions were determined by a rebreathing technique.

Although carbon dioxide production (\dot{V}_{CO_2}) was slightly greater in hypercapnic patients, the correlation between \dot{V}_{CO_2} and P_{CO_2} was not statistically significant. The correlations between P_{CO_2} and ventilatory parameters are shown in table 3. Minute volume was correlated with P_{CO_2} , but the correlation was not close. There was a closer relationship of P_{CO_2} to fractional physiological dead space ventilation. However, the inverse relationship between tidal volume and P_{CO_2} is even more striking, and there is a significant positive correlation between respiratory rate and carbon dioxide tension. If one estimates anatomical dead space as 175 ml., there is a +.72 correlation coefficient between fractional anatomical dead space ventilation and P_{CO_2} . When this effect is taken into account, the remainder of the physiological dead space ventilation (called alveolar dead space in table 3) shows no relationship to P_{CO_2} . Thus, hypercapnia appears to be determined primarily by a rapid shallow ventilatory pattern that necessitates a high fractional anatomical dead space ventilation. This accounted for most of the tendency to CO₂ retention, the remainder being due to a slightly higher CO₂ production and a slightly lower overall minute ventilation in hypercapnic patients.

As seen in table 4, lung compliance was also closely related to carbon dioxide tension. This relationship was highly significant regardless of the respiratory rate at which compliance was measured and was evident even when static compliance values were approached or when specific instead of total compliance was

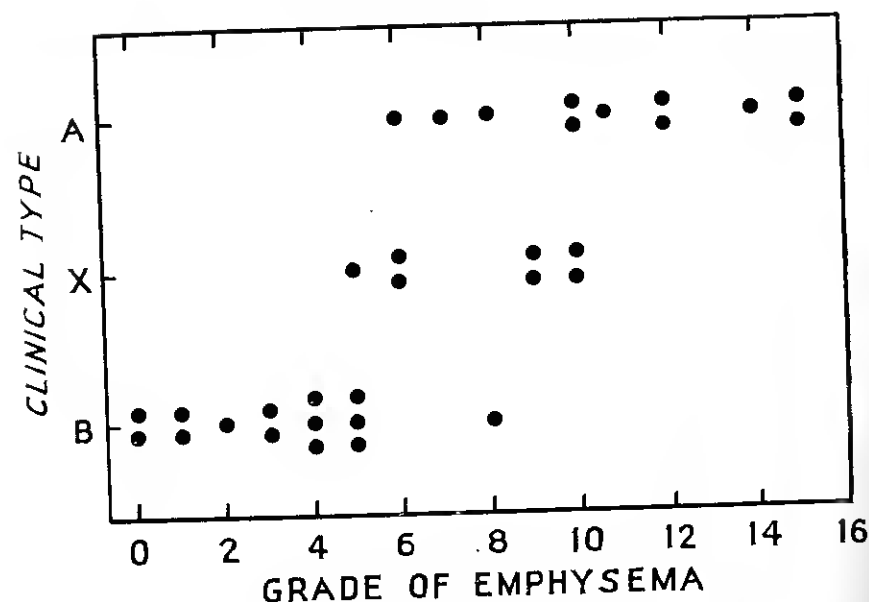


FIGURE 2. Anatomical emphysema in groups distinguished by the criteria outlined in the text.

considered. Differences between expiratory resistance of hypercapnic and normocapnic patients were generally not significant, but this may have been due, at least in part, to problems in quantitation. In contrast, inspiratory resistance did tend to be higher in hypercapnic subjects ($\bar{r} + .44$, $P < .05$).

We then examined the relationship between evidences of type A or type B disease and mechanical properties of the lung. Each patient received a score based on his diffusing capacity, lung volume, and sputum characteristics but without regard to CO_2 tension. The resultant A-B scores were then correlated with mechanical properties of the lung and with CO_2 tension. There was a highly significant correlation between A-B score and carbon dioxide level ($\bar{r} + .63$, $P < .001$). Correlations with mechanical properties are shown in table 6. Patients with predominantly type B features tended to have stiffer lungs. They also tended to have higher inspiratory resistances ($\bar{r} + .47$, $P < .05$ between inspiratory resistance and A-B score). However, there was no correlation of expiratory resistance measurements and A-B score, and examination of closed pressure-flow loops from the most typical type A and type B patients failed to reveal differences in their complex expiratory resistance characteristics.

TABLE 4.—Correlation of lung compliance with carbon dioxide tension and A-B score

Lung compliance	Versus CO_2 tension		Versus A-B score	
	Correlation coefficient	Probability	Correlation coefficient	Probability
Total lung compliance				
"Static".....	-.56	<.01	-.68	<.001
At $f = 20$	-.66	<.001	-.69	<.001
At $f = 100$	-.58	<.001	-.47	<.01
At resting f	-.62	<.001	-.61	<.001
Specific lung compliance				
"Static".....	-.40	<.05	-.57	<.01
At $f = 20$	-.54	<.01	-.51	<.01
At $f = 100$	-.52	<.01	-.34	<.05
At resting f	-.53	<.01	-.43	<.05

Compliance measurements were lower in typical type B patients at all breathing rates, and, as seen in figure 3, there was a similar percentile fall in measured compliance with increasing respiratory frequency in both types of disease. Differences in stiffness were apparent even when specific compliance was measured. The difference in compliance was not solely a function of difference in lung size.

Discussion and Summary

Although the story is far from complete, it is possible that many of the features that distinguish emphysematous patients (type A) and bronchial patients (type B) may be related to differences in the elastic property of their lungs.

The highly compliant lungs of the grossly emphysematous patients, by allowing a deep, slow breathing pattern, may minimize the ventilation wasted on the anatomical dead space and thereby help maintain adequate alveolar ventilation until late in the disease. This would tend to preserve more normal blood gases in these patients and would delay the development of polycythemia and pulmonary heart disease.

On the other hand, the more rapid, shallow ventilatory patterns of bronchial type patients would tend to aggravate blood gas

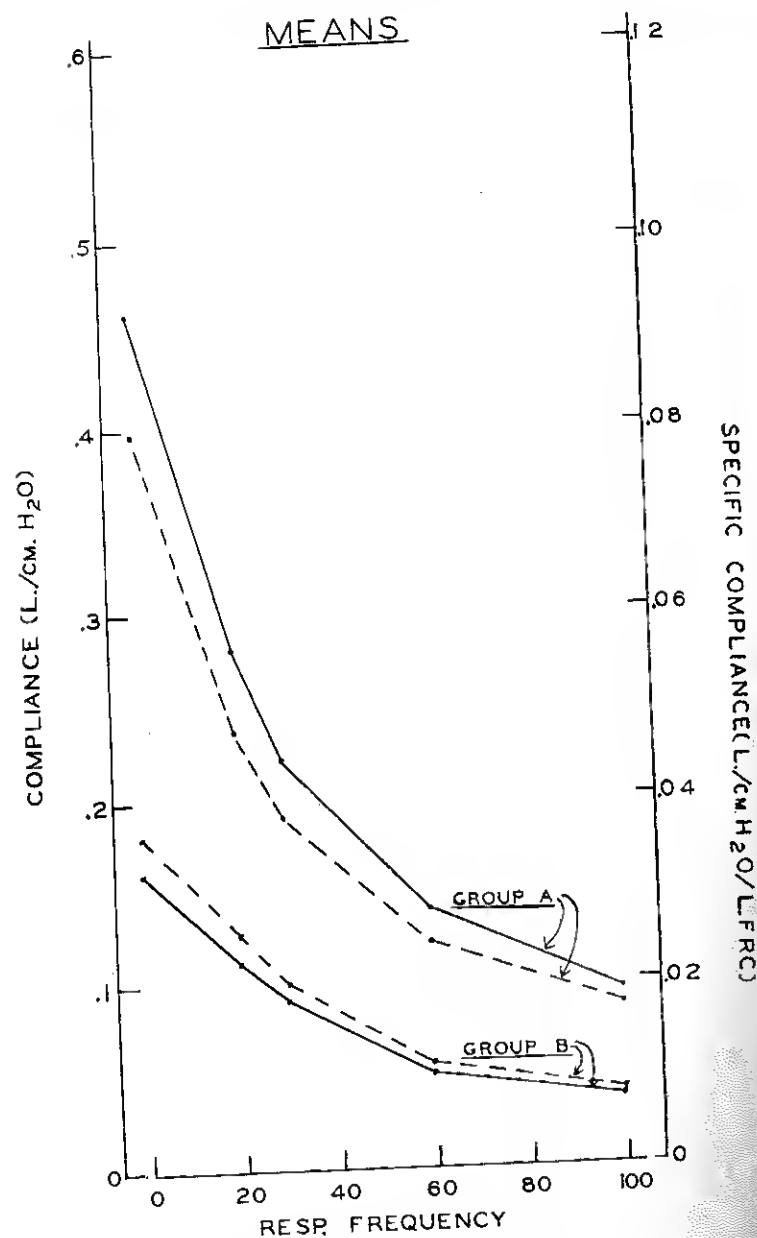


FIGURE 3. Mean total lung compliance (solid line) and specific lung compliance (broken line) in 5 patients with the lowest A-B scores (Group A) and 7 patients with the highest A-B scores (Group B). Group A contains the most typical type A patients, and Group B contains the most typical type B patients.

abnormalities and perhaps lead to the early development of cor pulmonale and congestive heart failure. This type of mechanism is supported by the observation that there is only a relatively low order negative correlation between heart weight and emphysema grade, but there is a quite close negative correlation between carbon dioxide tension and anatomical emphysema. In turn, there is a close correlation between carbon dioxide tension and heart weight ($\bar{r} + .56$). Thus, the association of findings suggests that type B patients are likely to develop hypercapnia and that hypercapnic type B patients are, in turn, likely to develop cardiac disease.

The data would support the concept that bronchial type B patients have a lesion situated primarily in or adjacent to the airways. The high inspiratory resistance of such patients, their frequent chronic productive cough, and their lack of anatomical emphysema would tend to support this concept. To what extent the entity is related to ordinary "chronic bronchitis" and to the Reid type of morphological change remains uncertain. For this reason, it seems preferable to designate these patients as bronchial rather than bronchitic in type. It also seems likely that parenchymal inflammatory changes are sometimes of importance in the pathogenesis of this type of disease, both by lowering lung compliance and by comprising the pulmonary vascular bed.

In contrast, the physiological abnormalities in the emphysematous type of patient may be explainable entirely by their anatomical emphysema, with consequent loss of support for the smaller airways. Since the susceptibility to intrinsic bronchial disease is likely to be increased by any anatomical emphysema that is present, it is not surprising that a clean, absolute separation of patients is difficult to obtain. Also, it is certainly quite possible, though as yet unproved, that emphysematous changes may occur as a consequence of a primarily bronchial type of disorder, or that both types of change may have common etiological factors.

It should be emphasized that individual patients with chronic airways obstruction present complex anatomical and physiological alterations that may vary with the stage of the disease and with acute exacerbations. The fact that it is often possible to distinguish the most emphysematous patients from the least emphysematous patients does not imply that there are two independent and distinct disorders. Nor does it imply that specific physiological patterns are completely restricted to patients with one or another type of underlying pathological alteration. Indeed, especially in

mild cases, it is very frequently impossible to determine the nature of the underlying pathology from clinical and physiological findings.

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EMPHYSEMA AND CHRONIC BRONCHITIS: CLINICAL MANIFESTATIONS AND THEIR PHYSIOLOGICAL SIGNIFICANCE

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Six major manifestations of bronchitis and emphysema are cough, dyspnea, cyanosis, pulmonary hypertension, polycythemia, and heart failure. Whereas all of these have a physiological basis, none can be understood completely when described in physiological terms alone, especially if these terms are restricted to the numbers emerging from pulmonary function laboratories.

Each of these manifestations is associated with certain general misconceptions, many of which have arisen from the use, in the study of these diseases, of the so-called multidisciplinary approach which, valuable as it may be, carries certain dangers as well. Basic clinical observations tend to be submerged by the flood of numerical data from the physiology laboratory, and some clinicians are unduly impressed by numerical data. When the physician observes that chronic productive cough is by far the most common early manifestation of chronic airway obstruction and considers this part of a disease, "chronic bronchitis," he should not be unduly influenced by physiologists who may claim that the patient's disease is really emphysema. (An increased RV/TLC usually indicates only airway obstruction and not necessarily emphysema.)

Pathologists also should be jealous of their right (and duty) to state, on the basis of their own criteria, that they find or do not find evidence of the airway obstruction the clinicians insist must be the main cause of the patient's death. (Such obstruction may be purely dynamic and not reflected in histological changes.) Physiologists, armed with their numbers, must not consider that, when the arterial oxygen tension has been measured, all that there is to know about the patient's oxygenation is thereby

Medical Clinics of North America has also published the major findings reported here (51: 283, 1967).